

## REMARKS

### 1. Claims Pending

Claims 1-8 were pending. Claim 8 has been withdrawn as being directed to non-elected subject matter. Thus, claims 1-7 are now pending and under consideration.

### 2. Claim Rejections Under 35 USC 112

(a) Claim 1 has been rejected under 35 USC 112, first paragraph because, the action asserts, this claim is directed to compounds wherein X is a sulphur atom whereas the specification is enabling only for compounds wherein X is an oxygen atom.

To overcome this ground of rejection claim 1 has been amended so that it is no longer directed to compounds wherein X is a sulphur atom.

(b) Claim 1 has also been rejected under 35 USC 112, first paragraph because, the action asserts, the scope of the phrase “a prodrug group” is not adequately enabled.

To overcome this ground of rejection claim 1 has been amended by replacing the phrase “a prodrug group” with “a C<sub>1-4</sub>-alkoxycarbonyl or C<sub>2-4</sub>-alkanoyl group”. Support for this replacement is found in the specification at page 2, lines 22-23, which states, “R<sub>1</sub> denotes a hydrogen atom or a prodrug group such as a C<sub>1-4</sub>-alkoxycarbonyl or C<sub>2-4</sub>-alkanoyl group”. In view of this descriptive support, the amendment does not introduce new matter.

(c) Claims 1, 2 and 6 have been rejected under 35 USC 112, second paragraph, as being indefinite.

(1) Claim 6 is rejected, because, the action asserts, it is a substantial duplicate of claims 1-5. The rejection of claim 6 for this reason is respectfully traversed because it is not supported by fact. Claims 1-5 are directed to compounds of formula I or salts thereof, including salts that are not physiologically acceptable. Claim 6, which depends from claims 1-5, is limited to salts of formula I that are physiologically acceptable. Thus, claim 6 contains a substantive limitation not found in claims 1-5, and it is not, therefore, a substantial duplicate of claims 1-5.

(2) Claims 1 and 2 are rejected because, the action asserts, inclusion of the phrase “group which can be cleaved in vivo” render the metes and bounds of the claims unclear.

It should be noted that the phrase in question appears in slightly different contexts in claims 1 and 2.

In claim 1, the phrase in question is included as part of a clause, which reads: “the hydrogen atom of any carboxy group present or a hydrogen atom bound to a nitrogen atom may each be replaced by a group which can be cleaved *in vivo*”. Thus, in claim 1, there are two situations wherein a hydrogen atom can be replaced by a group that can be cleaved *in vivo*. The hydrogen atom may either be that of a carboxy group or it may be bound to a nitrogen atom (as in an imino or amino group).

To overcome this ground of rejection, claim 1 has been amended by replacing the portion of the phrase which reads “a hydrogen atom bound to a nitrogen atom may ... be replaced a group which can be cleaved *in vivo*” by the following:

“and wherein a hydrogen atom bound to a nitrogen atom may each be replaced by hydroxyl, benzoyl, pyridinoyl, formyl, acetyl, propionyl, butanoyl, pentanoyl, hexanoyl, allyloxycarbonyl, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, tert.butoxycarbonyl, pentoxycarbonyl, hexyloxycarbonyl, octyloxycarbonyl, nonyloxycarbonyl, decyloxycarbonyl, undecyloxycarbonyl, dodecyloxycarbonyl, hexadecyloxycarbonyl, benzyloxycarbonyl, phenylethoxycarbonyl, phenylpropoxycarbonyl, C<sub>1-3</sub>-alkylsulphonyl-C<sub>2-4</sub>-alkoxycarbonyl, C<sub>1-3</sub>-alkoxy-C<sub>2-4</sub>-alkoxy-C<sub>2-4</sub>-alkoxycarbonyl or an R<sub>e</sub>CO-O-(R<sub>f</sub>CR<sub>g</sub>)-O-CO group wherein

R<sub>e</sub> denotes a C<sub>1-8</sub>-alkyl, C<sub>5-7</sub>-cycloalkyl, phenyl or phenyl- C<sub>1-3</sub>-alkyl group,

R<sub>f</sub> denotes a hydrogen atom, a C<sub>1-3</sub>-alkyl, C<sub>5-7</sub>-cycloalkyl or phenyl group and

R<sub>g</sub> denotes a hydrogen atom, a C<sub>1-3</sub>-alkyl or R<sub>e</sub>CO-O-(R<sub>f</sub>CR<sub>g</sub>)-O group wherein R<sub>e</sub> to R<sub>g</sub> are as hereinbefore defined,

or wherein an amino nitrogen may form part of a phthalimido group”

This new claim language, which is clear, is essentially to be found in the specification at page 14, lines 1-20. Thus, there is descriptive support in the specification for the new language and it does not constitute new matter.

To further overcome this ground of rejection, the portion of claim 1 which reads “the hydrogen atom of any carboxy group present ...may be replaced by a group which can be cleaved *in vivo*” has been replaced by the phrase “any carboxy group contained in the abovementioned groups may be replaced by a tert.butoxycarbonyl precursor group”. This new claim language, which is clear, is essentially to be found in the specification at page 34, lines 4-5. Thus, there is descriptive support in the specification for the new language and it does not constitute new matter.

In claim 2, the phrase “group which can be cleaved *in vivo*” is included in two separate clauses, which read:

“a hydrogen atom bound to a nitrogen atom in the abovementioned groups may be replaced by a group which can be cleaved *in vivo*,  
the carboxy groups contained in the abovementioned groups may each be substituted by a group which can be cleaved *in vivo*,”

Thus, in claim 2, there are again two situations wherein a hydrogen atom can be replaced by a group that can be cleaved *in vivo*. The hydrogen atom may either be that of a carboxy group or it may be bound to a nitrogen atom (as in an imino or amino group).

To overcome this ground of rejection, claim 2 has been amended by replacing the clause which reads “a hydrogen atom bound to a nitrogen atom in the abovementioned groups may be replaced by a group which can be cleaved *in vivo*,” by the following:

“a hydrogen atom bound to a nitrogen atom in the abovementioned groups may be replaced by hydroxyl, benzoyl, pyridinoyl, formyl, acetyl, propionyl, butanoyl, pentanoyl, hexanoyl, allyloxycarbonyl, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, tert.butoxycarbonyl, pentoxycarbonyl, hexyloxycarbonyl, octyloxycarbonyl, nonyloxycarbonyl, decyloxycarbonyl, undecyloxycarbonyl, dodecyloxycarbonyl, hexadecyloxycarbonyl, benzyloxycarbonyl, phenylethoxycarbonyl, phenylpropoxycarbonyl, C<sub>1-3</sub>-alkylsulphonyl-C<sub>2-4</sub>-alkoxycarbonyl, C<sub>1-3</sub>-alkoxy-C<sub>2-4</sub>-alkoxy-C<sub>2-4</sub>-alkoxycarbonyl or an R<sub>e</sub>CO-O-(R<sub>f</sub>CR<sub>g</sub>)-O-CO group wherein

R<sub>e</sub> denotes a C<sub>1-8</sub>-alkyl, C<sub>5-7</sub>-cycloalkyl, phenyl or phenyl- C<sub>1-3</sub>-alkyl group,  
 R<sub>f</sub> denotes a hydrogen atom, a C<sub>1-3</sub>-alkyl, C<sub>5-7</sub>-cycloalkyl or phenyl group and  
 R<sub>g</sub> denotes a hydrogen atom, a C<sub>1-3</sub>-alkyl or R<sub>e</sub>CO-O-(R<sub>f</sub>CR<sub>g</sub>)-O group wherein R<sub>e</sub> to R<sub>g</sub> are as hereinbefore defined,  
 or wherein an amino nitrogen may form part of a phthalimido group”.

Also to overcome this ground of rejection, claim 2 has been further amended by replacing the clause which reads “the carboxy groups contained in the abovementioned groups may each be substituted by a group which can be cleaved *in vivo*” with the clause “wherein any carboxy group contained in the abovementioned groups may be replaced by a tert.butoxycarbonyl precursor group.” This new claim language, which is clear, is essentially to be found in the specification at page 34, lines 4-5. Thus, there is descriptive support in the specification for the new language and it does not constitute new matter.

### 3. Claim Rejections Under 35 USC 103

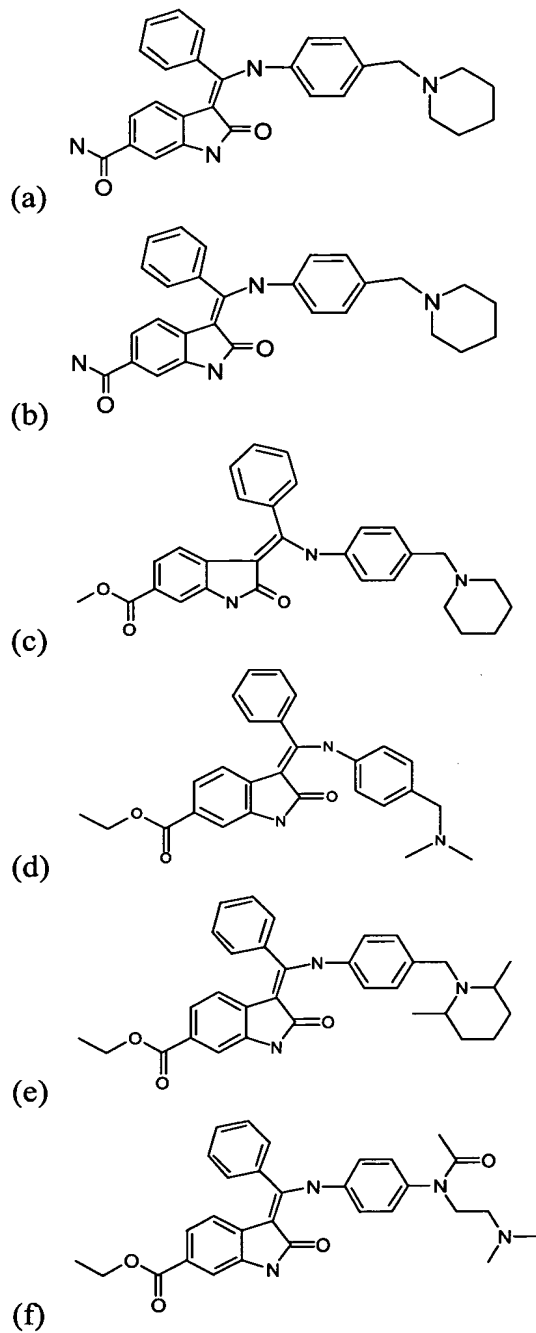
Claims 1-7 stand rejected under 35 USC 103(a) as being unpatentable over Davis et al. (WO 99/15500). The rejection of claims 1-7 on this basis is traversed for the reasons that follow.

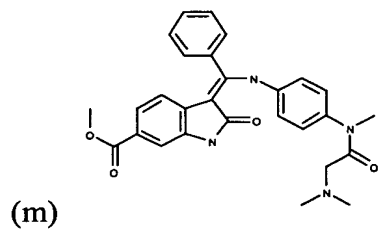
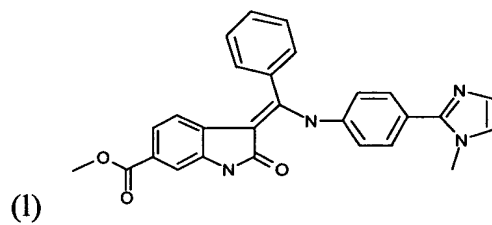
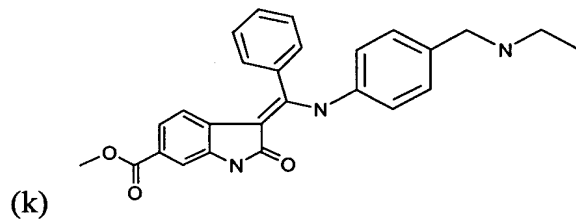
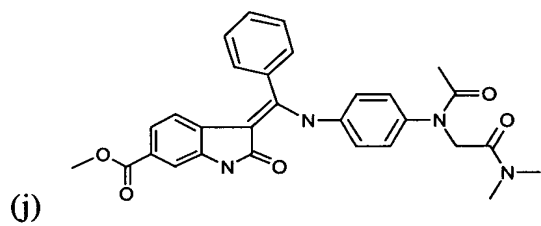
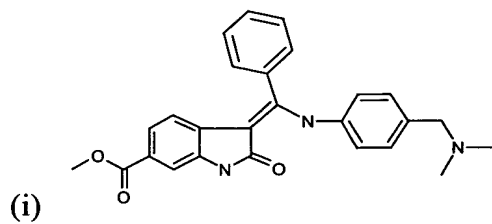
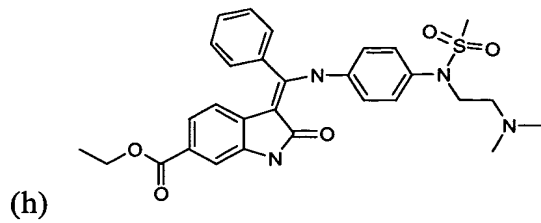
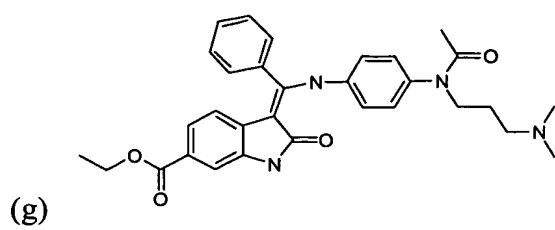
First, it is respectfully pointed out that the Examiner is believed to be in error in asserting that Davis et al. describe compounds of the formula I (given on page 5 of the reference) wherein R<sup>3</sup> is aliphatic aminocarbonyl. Rather, the reference, at page 6, line 14, describes compounds wherein R<sup>3</sup> is di-C<sub>1-12</sub> aliphatic aminocarbonyl.

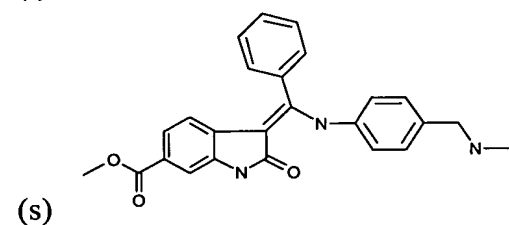
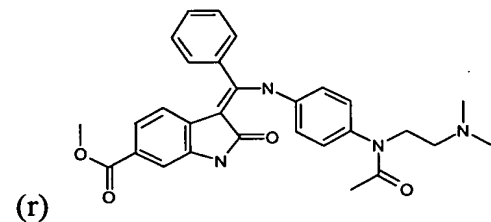
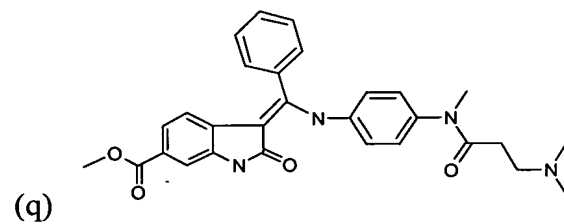
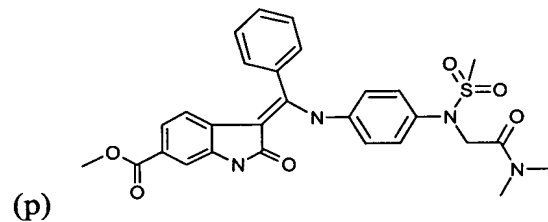
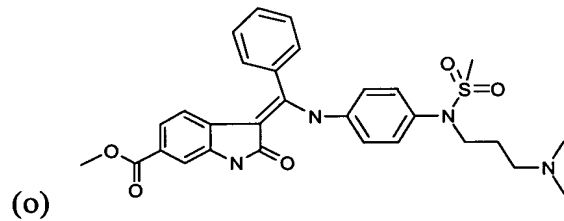
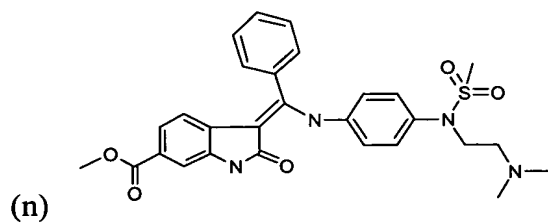
Next, it is pointed out that claims 1 and 2 have been amended by deleting from the definition of R<sub>2</sub> the clause “or, if R<sub>4</sub> does not denote an aminosulphonyl-phenyl or N-(C<sub>1-5</sub>-alkyl)-C<sub>1-3</sub>-alkylaminocarbonyl-phenyl group, it may also denote a di-(C<sub>1-2</sub>-alkyl)-aminocarbonyl group”. In view of this amendment, claims 1 and 2 no longer embrace compounds wherein R<sub>2</sub> can be a di-(C<sub>1-2</sub>-alkyl)-aminocarbonyl group. For this reason, claims 1 and 2 as amended do not embrace species of the genus taught by the reference. It follows

that claims 3 and 4, which depend from claim 1 and are narrower in scope, also do not embrace species of the genus taught by the reference. For this reason, it is respectfully asserted that claims 1-4 are patentable over the reference.

Claim 5 is directed to the following species.







It is respectfully asserted that none of the species of independent claim 5 fall within the genus taught by the reference. Thus, claim 5 should be patentable over the reference.

Claims 6 and 7 depend from claims 1-5. These should be patentable over the reference for the same reasons that claims 1-5 are patentable over the reference.

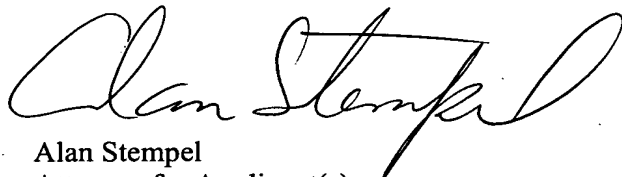
Based upon the foregoing, it is respectfully asserted that the rejection of claims 1-7 as

being unpatentable over Davis et al. is improper and the rejection of these claims should be withdrawn.

4. Information Disclosure Statement

The action asserts that the information disclosure statement filed on February 26, 2001 fails to comply with 37 CFR 1.98(a)(2). The action does not specify what requirement of 37 CFR 1.98(a)(2) has not been complied with. The undersigned believes that a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed in the information disclosure statement has been supplied to the office, as part of the submission of February 26, 2001. The Office has, by a return post card, acknowledged receipt of the same. The Examiner is asked to specify the documents that have not been supplied or which have been misplaced by the Office. Applicants will promptly provide a copy of any document so specified.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Alan Stempel".

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Enclosures: Fee Transmittal (one page)